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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/523,102	SI ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 71-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 71-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/6/05,11/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6, 71-113 are pending and are considered on the merits.

Double Patenting

The provisional obviousness-type double patenting rejection has been overcome by applicant's amendments in 09/648446 because the claims no longer are overlapping in scope.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 75-77, 87-89, 99-101, 110-113 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is difficult to understand how a mammal in need of prevention of retinal neovascularization in claims 88, 100, 112 can already have neovascularization due to neovascular glaucoma, ocular insults, ocular trauma or surgical injury or transplantation, etc.. Preventing means before the event occurs. A patient with diabetes or a patient who will have ocular surgery may be in need of preventing retinal neovascularization, but a patient who already has neovascularization cannot be "prevented" from having that condition. Applicants should carefully review the claims so that the dependent claims further limit the independent claims.

Also, "pterigium" is not a disease of retinal neovascularization and the correct spelling is pterygium, see attached reference [U]. Therefore, it cannot be said to further limit the requirements of claims 1, 78, 90 and 102.

Claims 77, 89, 101, 113 are also indefinite. The independent claims require preventing or treating **retinal** neovascularization. However, claims 77, 89, 101, 113 merely state that the condition be one where signals associated with angiogenesis are detected or new vessel growth can be detected or a

disease implicating MMP activity or endothelial invasion. This could be breast cancer, for example. It is suggested that a phrase such as "in the retina" be inserted in the logical places in the recitation of hypothetical conditions. The claims are indefinite because they attempt to expand the scope of the independent claim. Careful attention to the language of the pending claims without undue proliferation of the number of the claims would assist in the advancement of prosecution.

Also, please explain how a disease can implicate MMP activity? Perhaps a disease may have associated increases in MMP activity, but "implication" has many meanings. If applicants mean that MMP activity is a necessary consequence or is associated with the disease or is coupled to the production of MMP, please so state. Please explain the difference between "detected" and "observed" as used in claims 77, 89, 101, 113. There must be a difference else the word "detected" would suffice.

Claim 110 is improper because it does not further limit the independent claim which has the compound of formula (I), a polymeric suspension agent and one or more carriers....

Claims 75, 87, 99, 111 require that the compound not be batimastat. However, in lines 3 and 5 of claims 1, 78, 90, 102, applicants use the term "a batimastat compound". The use of the term, batimastat for both a generic group and a species is indefinite and confusing. Please consider canceling the word "batimastat" in the independent claims and inserting "of the formula (I). Please then amend claims 3, 80, 92, 104 to have proper antecedent basis.

Claim Rejections - 35 USC § 102

Claims 78-86, 90-98, 102-110 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,767,153 (of record).

The claims are directed to the one step method of **preventing** retinal neovascularization by topically administering to the eye a composition

comprising a polymeric suspension agent and consisting essentially of a (0.01-3% w/w) batimastat compound of the claim specific formula. The mammal which is the recipient of this administration is a mammal which is susceptible to developing retinal neovascularization.

US 5,767,153 teaches the topical administration to a recipient of a composition comprising batimastat (0.3 weight %) and polycarbophil (1.15 weight %). See Example 7, Table I. Since everyone is susceptible to developing retinal neovascularization by developing the diseases of the retina and/or traumatic ocular insults as described on page 1 of the instant specification, and no specific type of recipient is required by the claims, the recipient is interpreted to be the same as the recipient of the claims. As the composition administered is the same (batimastat and polycarbophil), the concentrations of the components of the composition is the same and the patient required is the same, the inherent result of the one method step would be the same, that is prevention of retinal neovascularization.

See Titanium Metals, 778 F.2d at 775. In Titanium Metals, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." Titanium Metals, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting that "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." Id. at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art. The public remains free to make, use, or sell prior art compositions ***or processes***, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other

doctrines, enforces that basic principle." See Atlas Powder Co. v. IRECO Inc. 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the "natural result" flowing from the reference's explicitly explicated limitations. Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

It is not relevant to the analysis of the claimed method that the reference makes no mention of (inhibiting, preventing etc.). Discovery of a new benefit for an old process does not render the old process patentable. In re Woodruff, 919 F. 2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). Merely because the reference did not have one of applicant's purposes in mind when the (drug was administered) does not alter the drug's physiological activity. In the context of an anticipation rejection, the Federal Circuit stated, "Where, as here, the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results." Mehl/Biophile Int'l Corp. v. Milgraum, 192 F. 3d 1362, 1366, 52 USPQ2d 1303, 1307 (Fed. Cir. 1999).

See also In re Cruciferous Sprout 64 USPQ2d 1202 Fed. Circuit, where the Federal Circuit upheld a decision that patents licensed to Brassica Protection Products, Inc. are invalid because they are anticipated by the prior art. The patents are for method of growing and eating certain sprouts to reduce the level of carcinogens in animals, thereby reducing the risk of developing cancer. Prior art references disclose growing and eating those specific sprouts. The Federal Circuit cited authority for the rule that "a prior art reference may anticipate when the claim limitations not expressly found in the that reference are nonetheless inherent in it." The court said, "While Brassica may have recognized something quite interesting about those sprouts, it simply has not invented anything new.".

See also Ex parte Novitski, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) The board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of P. cepacia. A US patent to Dart disclosed inoculation using P. cepacia bacteria for protecing the plant from fungal disease. Dart was silent with regard to nematode inhibition, but the Board concluded that nematode inhibition was an inherent property of the bacteria, and therefore of the method as disclosed by Dart.

Response to Arguments

Applicants argue that the examiner has not shown that the result of the methods of '153 necessarily prevent retinal neovascularization. Since the claimed one step method of administering the same agent in the same fashion is the same method as taught in the prior art, the result would inherently be the same. If applicants' claimed method prevents neovascularization, the method practiced in '153, which is the same method would also prevent neovascularization. This is a natural result flowing from the reference's explicitly explicated limitations of the one step administration method. Applicants argue that just because a mammal is susceptible to a condition does not mean that they are in need of prophylaxis. Since the term, prophylaxis means measures designed to preserve health [V], all persons need to preserve health by preventing neovascularization, especially with regard to ocular insults. While the claims to employing the prophylactic method on a patient with diabetes may not be anticipated, no disease condition is mentioned in the method as claimed.

Claim Rejections - 35 USC § 103

Claims 1-6, 71-74, 76-86, 88-98, 100, 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,767,153 [A] in view of WO 97/41844 [N].

The claims are directed to a one step method of treating or preventing retinal neovascularization in an animal comprising topically administering a

composition comprising (0.01-3% w/w) batimastat and in some of the claims, a polymeric suspension agent, particularly polycarbophil.

The references are relied upon as explained below.

US 5,767,153 discloses a composition comprising 0.3% batimastat and 1.15% polycarbophil useful for topical ophthalmic administration, (col. 2, l.7 and example 7). It teaches that inclusion of medicaments such as batimastat in combination with polycarbophil increases its bioavailability to the target tissue in the eye (col. 2, ls. 19-21).

The reference lacks the disclosure of use of the composition of polycarbophil and batimastat for the treatment of retinal neovascularization.

WO 97/41844 discloses that batimastat is an angiostatic agent (Table 1) and as such is effective in compositions for the treatment of diseases where neovascularization arises such as diabetic retinopathies, proliferative virtreoretinopathies and other diseases (page 1, second paragraph and page 5, table 1). Compositions comprising at least two angiostatic compounds and particularly containing metalloproteinase inhibitors such as batimastat, which is a preferred angiostatic agent (page 19, l. 9) are in topical ophthalmic formulations (claim 20 and Example 1). The compositions include a polymeric suspension agent, for example tyloxapol (Example 1) or suspensions using viscous or semi-viscous gels or other types of semi-solid compositions (page 22, lines 8-14). The compositions may be used to prevent retinal neovascularization (page 20, l. 11).

The substitution of the polycarbophil suspension agent disclosed in US 5,767,153 for the generic suspension agent such as a gel or the specifically exemplified tyloxapol suspension agent with the two angiostatic compounds, one of which may be batimastat, taught in the topical ocular treatment method of WO 97/41844 would have been obvious because batimastat is a known MMP inhibitor and is known to be useful to treat retinal neovascularization as taught

in '844. The formulation of batimastat with polycarbophil as a suspension agent is taught in '153 to be particularly advantageous in terms of delivering a sustained dosage of a sparingly water soluble active ingredient such as batimastat over time.

One of ordinary skill in the art would have been motivated at the time of invention to substitute a the suspension agent tyloxapol in the two angiostatic component composition of WO 97/41844 for the suspension agent polycarbophil as taught in '153 to treat retinal neovascularization in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Claims 75, 87, 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,767,153 [A] in view of WO 97/41844 [N].
as applied to claims 1-6, 71-74, 76-86, 88-98, 100, 101 above, and further in view of US 5,917,090 [AK2] already of record.

US 5,917,090 disclose compounds of formula I which fall within applicants' formula but does not include batimastat. These compounds are stated to be matrix metalloproteinase inhibitors and useful for treating angiogenesis dependent (neovascularization) diseases including retinopathy and neovascular glaucoma (col. 1, l. 26-30).

The substitution of the MMP activity inhibitors disclosed in '090 for the specific MMP activity inhibitor, batimastat would have been obvious when taken with '844 which teaches the use of a composition of two angiostatic compounds, of which MMP activity inhibitors such as batimastat are preferred compounds and a polymeric suspension agent such as tyloxapol for topical application to the eye for treatment of neovascularization.

Response to Arguments

Applicants argue that the term "consisting essentially of a polymeric suspension agent and a batimastat compound of the formula..." overcomes the '844 reference. Please note that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz , 537 F.2d 549, 551 - 52, 190 USPQ 461, 463 (CCPA 1976)

When an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of", applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). In the instant case, the characteristics of the composition used in the claimed method are still the same as the characteristics of the composition in the prior art reference of '844. That is, the composition has MMP inhibitor activity, of which batimastat is one of the preferred MMP inhibitors and it can be topically applied to the eye to treat neovascularization.

Applicant argues that there is no motivation to combine references because the claims recite "consisting essentially of a polymeric suspension agent and a batimastat compound", while the reference of '844 is directed to the use of two angiostatic agents (of which batimastat is a preferred and a preferred polymeric suspension agent is tyloxapol). Please note above, the comments about the meaning of the term, "consisting essentially of" which is construed as equivalent to comprising absent a clear indication of what the novel and basic characteristics actually are and how the inclusion of another angiostatic agent in the composition would materially change applicant's invention. See MPEP 2111.03

Allowable Subject Matter

A claim drawn to **treating** retinal neovascularization in a mammal comprising topically administering to the eye a suspension consisting of the

compound of formula 1 (batimastat), a polymeric suspension agent, and one or more carriers... etc., might be found to be allowable upon presentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is 571-272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sandra Saucier
Primary Examiner
Art Unit 1651